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EXAMINER	
LAM, ANN Y	

ART UNIT	PAPER NUMBER
1641	

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07/25/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/768,742	TERPETSCHNIG ET AL.	
	Examiner	Art Unit	
	ANN Y. LAM	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _07 April 2008_.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _28-30,33-41,83,84,88 and 89_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _28-30, 33-41,83,84, 88, 89_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application

6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 83, 28-30, 37-41, 88 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laing et al., 6,331,392, in view of Hainfeld et al., 5,521,289.

As to independent claim 83, Laing et al. discuss fluorescence polarization and disclose that the degree to which the fluorescence emission vector moves is directly related to the mobility of the fluorescently labeled molecule. If the fluorescently labeled molecules are large, they move very little and the emitted light remains highly polarized with respect to the excitation plane. In contrast if the fluorescently labeled molecules are small, they rotate or tumble faster, and the resulting emitted light is depolarized relative to the excitation plane (col. 8, lines 45-54.) Moreover, Laing et al. teach in an embodiment, an RNA target conjugated to a larger molecule, such as streptavidin via a biotin attached to the target RNA, thereby enhancing differences in polarization of the fluorescent probe subsequent to ligand binding (col. 9, lines 44-50).

Moreover, while neither Laing et al. nor Hainfeld et al. teach mass labeling the *product* as opposed to either initial reagent (Laing et al. teach attaching the large

molecule, which is essentially a mass label, to the target, and fluorescently labeling the probe), the skilled artisan however would recognize that the fluorescently labeled complex increases in size upon formation of the product from the reaction, which in turn enhances the difference in polarization before and after a reaction as discussed by Laing et al. Moreover, it is predictable by the skilled artisan that providing a mass label that binds only to the product and not to the initial reagents (e.g., an enzyme substrate) and fluorescently labeling the substrate also produces the same result of increasing the size of the labeled complex (e.g., the labeled substrate) to enhance the difference in polarization before and after a reaction, and such predictability renders the technique obvious. Also, the skilled artisan would recognize that performing an assay to detect the product of an enzyme-substrate reaction is known and desirable, and thus, tailoring the technique discussed above to detect specifically a product of an enzyme-substrate reaction would also have been within the skills of the ordinary artisan. The fluorescent label discussed by Laing et al. is equivalent to Applicant's claimed luminophore and the particle discussed by Hainfeld et al. is equivalent to Applicant's claimed mass label.

However, Laing et al. do not disclose using a bead complex (e.g., streptavidin-bead conjugate) as an alternative to the streptavidin alone, as a means for enhancing differences in polarization subsequent to binding.

Hainfeld et al. however teach that discuss that in a particular assay using piezoelectric detect, having a surface with an antigen, when an antibody binds to this surface, the additional molecule changes the mass slightly which can be detected via a frequency change. Moreover Hainfeld et al. teach that by using, e.g., gold conjugates,

such as colloidal particles with covalent antibodies attached, a “sandwich” can be formed and the large mass of the gold will greatly amplify the signal making detection levels far lower. Hainfeld et al. further teach that a related technique uses reflection of light from a surface. When the surface is coated with a layer of antibodies there is a change in the peak reflection angle. Use of the metallic particles as just described will influence to a far greater extent the change in reflection due to the strong optical properties of gold or other metal particles used. Choice of wavelength, polarization and optimizing other parameters for metal particle interaction and detection can further enhance the sensitivity. See column 6, lines 34-58.

While Laing et al. teach attachment of a target to a larger molecule to decrease mobility to enhance the difference in polarization before and after ligand binding, but do not disclose using a particle to decrease mobility, the skilled artisan would have been suggested to do so by the Hainfeld et al. reference since Hainfeld et al. teach that a particle will add mass, which as the skilled artisan would understand would decrease mobility. While Hainfeld et al. disclose this increase in mass as an enhancement of detection in a detection technique that is different from the Laing et al. polarization technique, the skilled artisan would nevertheless have reasonable expectation of success since the same principle would apply in a polarization assay, that is, the particle will add mass (as disclosed by Hainfeld et al.), and the mass will decrease mobility thus enhancing the difference in polarization before and after ligand binding, as discussed by Laing et al., as would be desirable for enhancing sensitivity of the detection.

As to claim 28, the fluorescent label is inherently photoluminescent.

As to claim 29, neither Laing et al. nor Hainfeld et al. teach that the additional limitations recited in claim 29. However, whether the photoluminescence lifetime is greater than the rotational correlation time of the unbound probe (luminophore) and less than the rotational correlation time of the complex formed by binding of the substrate to the mass label depends on what fluorescent moiety is used and what choice of enzymes and substrates are used. Moreover, the photoluminescence lifetime as claimed by Applicant appears to be an optimum or workable range. It has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art (see MPEP 2144.05 IIA, citing In re Aller, 105 USPQ 233.)

As to claim 30, Laing et al. disclose an RNA target conjugated to a larger molecule, such as streptavidin via a biotin attached to the target RNA, thereby enhancing differences in polarization of the fluorescent probe subsequent to ligand binding (col. 9, lines 44-50). Such binding between streptavidin and biotin is well known in the art, and it is well within the knowledge of the skilled artisan to utilize various known binding partners, such as streptavidn and biotin (which noncovalently bind to each other) to bind materials of interest, such as the luminophore (fluorescent molecule) to the enzyme substrate.

As to claim 37, the luminophore is not normally present in the sample. (The Office notes that this is a recitation of intended use. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed

invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, such as in this case, then it meets the claim.)

As to claim 38, the mass label is not normally present in the sample (The Office notes that this is also a recitation of intended use, and the prior art structure is capable of performing the intended use.)

As to claim 39, the property of the luminophore is related to a rotational diffusion coefficient of the luminophore. It is noted that Applicant does not specify what property of the luminophore, therefore the claim encompasses any property of the luminophore, including its polarization.

As to claim 40, the property may be measured using polarization (see Laing et al.., col. 9, lines 44-50).

As to claim 41, the property of the luminophore is related to the translational diffusion coefficient of the luminophore. It is noted that Applicant does not specify what property of the luminophore, therefore the claim encompasses any property of the luminophore, including its polarization.

As to claim 88, the mass label (particle) is capable of binding specifically to the product, and the luminescence property of the luminophore is different for the luminophore bound to the substrate than for a complex of the luminophore, the product, and the mass label (see discussion of claim 83 above).

As to claim 89, the luminescence property may be measured using fluorescence polarization (see discussion of claim 83 above.)

Claims 33-36 and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Laing et al., 6,331,392, in view of Hainfeld et al., 5,521,289, as applied to independent claim 83 above, and further in view of Yguerabide et al., 6,586,193.

Laing et al. in view of Hainfeld et al. have been discussed (see discussion of independent claim 83 above). Neither Laing et al. nor Hainfeld et al. however disclose a mass label comprising a plurality of binding moieties that are capable of binding to the products (as recited in claim 33), or the mass label being a first mass label and the method further comprising a second mass label that is capable of binding to the product or first mass label or a combination thereof but not the luminophore alone (as recited in claim 34).

However, Yguerabide et al. teach aggregating or cross-linking of beads produced by the presence of an analyte can be detected in polarization assays (col. 84, lines 26-41). Yguerabide et al. teach that these assays involve the association or aggregation of two or more particles by interaction of analyte and specifici analyte recognition reagents, and that it is known in the art that by using the appropriate binding agents and concentration of binding agents and analyte (for example an antigen that is multivalent), agglutination, aggregation, cross-linking, networking and similar binding events can occur and that these events can be used to detect one or more analytes in a sample. Yguerabide et al. disclose that for example visible precipitates are formed if the antigen

is soluble and multivalent (col. 83, lines 53-59. Moreover, Yguerabide et al. teach that the disclosed invention allows for easier use, more sensitive and versatile detection of analytes and that the type of aggregates formed depends on the size of the cross-linking agents and their valency and the type of binding agent attached to the particle (col. 84, lines 1-11.) The skilled artisan would thus recognize that using multiple probes on a bead and/or probes for a multivalent analyte in the invention of Laing et al. as modified by Hainfeld et al. will produce such cross-linking as disclosed by Yguerabide. The skilled artisan would have been motivated to provide for such cross-linking in the Laing et al.-Hainfeld et al. invention because Yguerabide et al. teach that this allows for the advantages of easier use, more sensitive and versatile detection of analytes.

As to claim 35, Yguerabide et al. disclose that aggregates formed can comprise two particles to many (col. 84, line 11) (see also for example col. 88, lines 3-12). Thus Yguerabide et al. disclose a network of for example three mass labels (a second mass label bound to two first mass labels, as recited by Applicants

As to claim 36, Yguerabide et al. teach that the second mass label includes at least biotin (col. 88, lines 3-12). (The Office notes that although Yguerabide et al. teach that the second mass label includes biotin indirectly, through linkage with streptavidin, the claim nevertheless read on this disclosure.)

As to claim 84, Yguerabide et al. disclose that beads of various materials may be used, such as glass beads. Using beads comprising glass in the Laing et al.-Hainfeld et al. invention would have been within the skills of the ordinary artisan as Yguerabide et al. disclose such materials for use as assay beads. The skilled artisan would have

reasonable expectation of success as the glass beads will also increase mass and thus decrease mobility, which would enhance polarization detection (as taught by Laing et al.)

Response to Arguments

Applicant's arguments filed April 7, 2008 have been fully considered. Applicant asserts that the Sportsman et al. reference is not prior art. Applicant's arguments are persuasive. The grounds for rejection has been amended to cite Hainsfeld et al. to teach particle labeling to increase mass for enhancing detection techniques. Thus, Applicant's arguments are moot in view of the new grounds for rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/

Primary Examiner, Art Unit 1641